



Adult Vitamin D Deficiency: Review of the Literature and Implications for

Force Health Protection

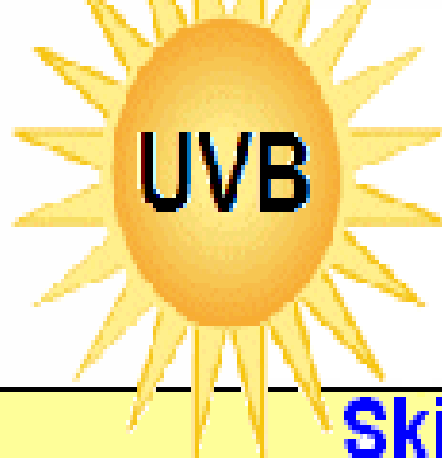
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Deployment Health Clinical**

Objectives



- ♠ **“Bare Bones” Overview of Vitamin D**
 - Physiology and Epidemiology of Vitamin D Deficiency
- ♠ **Is there Evidence for Vitamin D Deficiency in the Military?**
 - **Risk for Stress Fractures, a Force Health Protection Concern**
 - Finnish Male Recruits
 - U.S. Navy Female Recruits
 - **Vitamin D Deficiency at the Deployment Health Clinical Center**
 - Two Case Studies
 - Results from screening of 83 service members with nonspecific chronic musculoskeletal pain
- ♠ **Beyond “the Bare Bones”**
 - More Vitamin D Physiology—Chronic Pain, Cancer, Anxiety
- ♠ **Supplementation for Vitamin D Deficiency**
- ♠ **Conclusions**



80%

Skin

7-Dehydrocholesterol



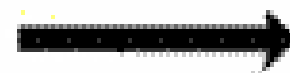
Pre Vitamin D3

Diet:

20%

Vitamin D2

Vitamin D3



Vitamin D



Liver

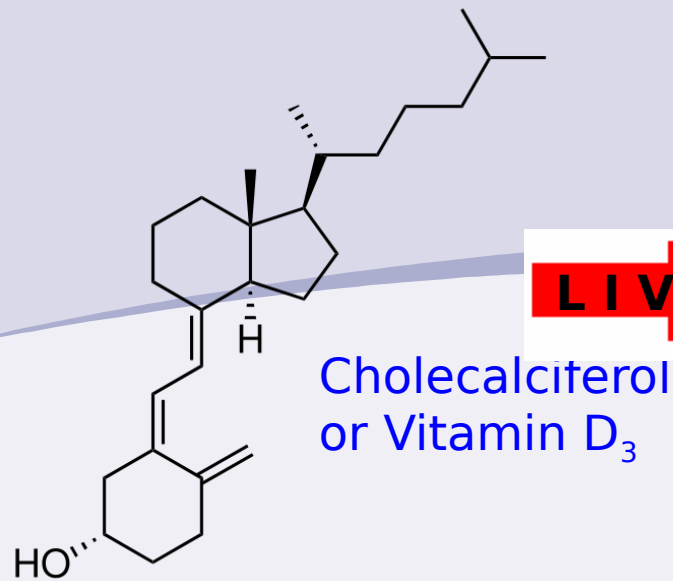
25 Hydroxylase

CYP3A4

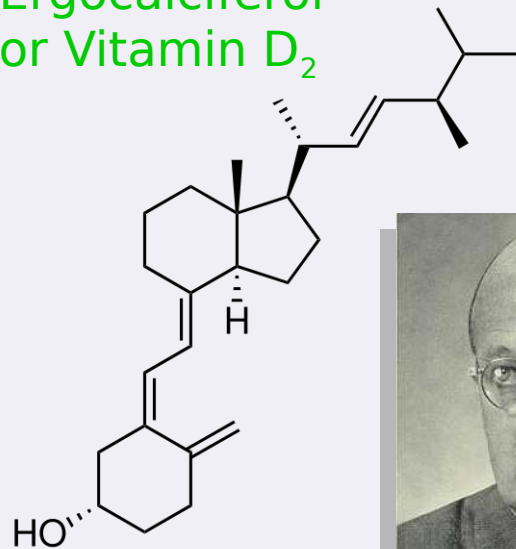


25 Hydroxyvitamin D

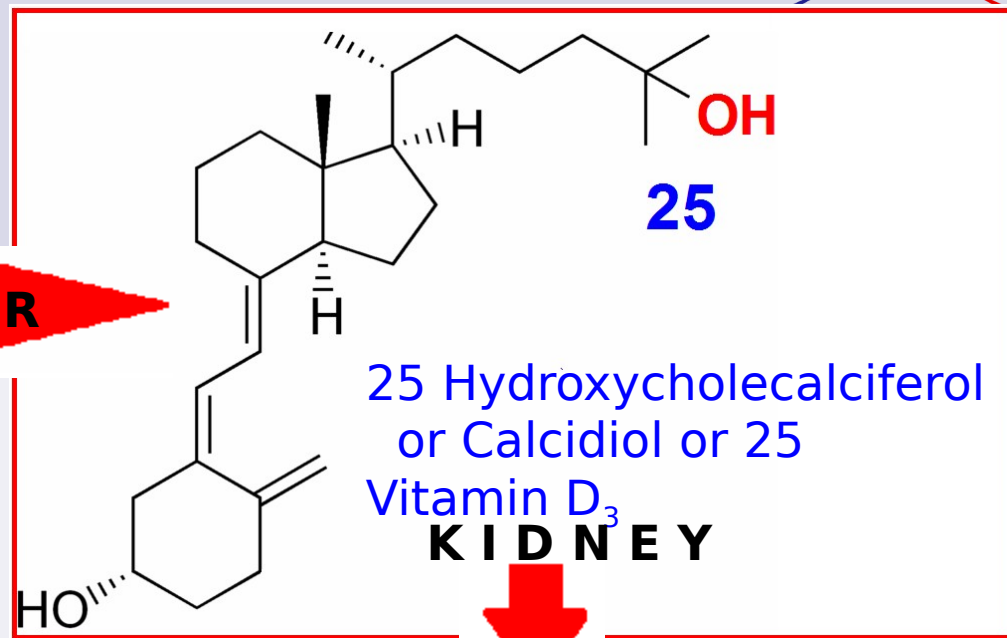
LIVER



Ergocalciferol
or Vitamin D₂



C



KIDNEY

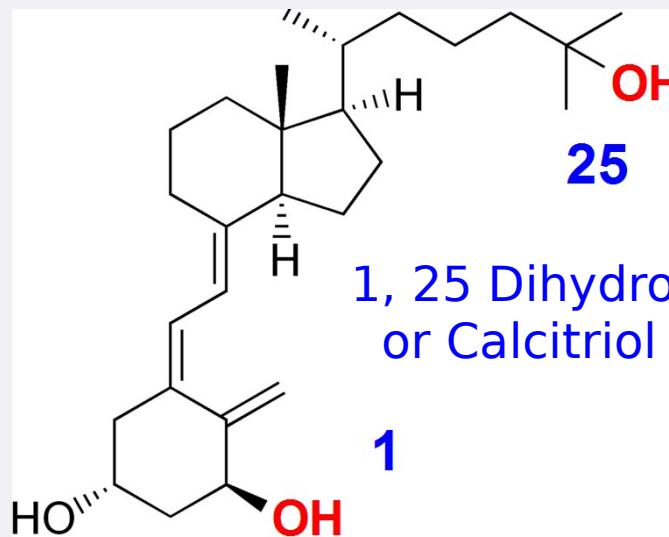
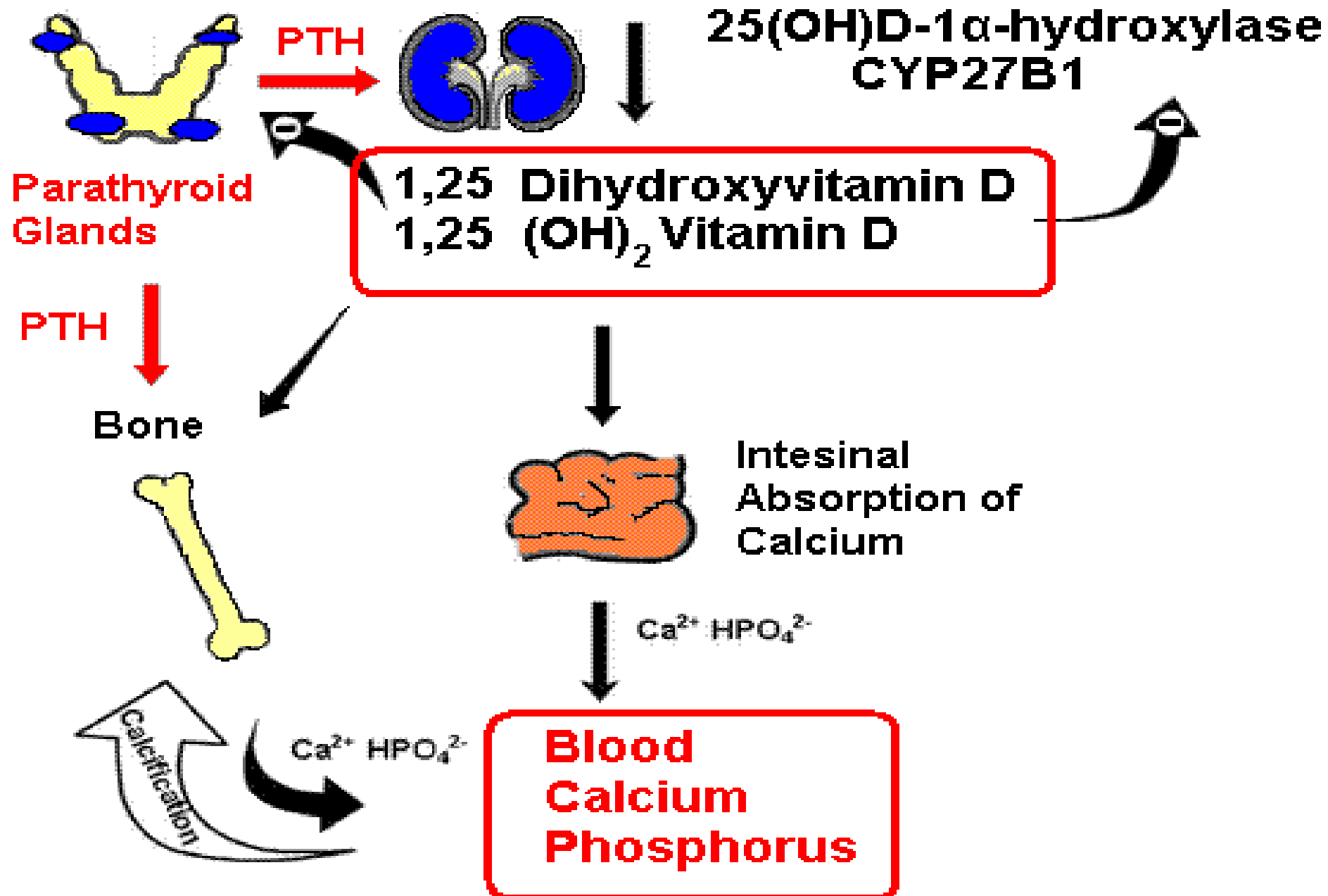


Photo and modified chemical structures from Wikipedia Co

25 Hydroxyvitamin D



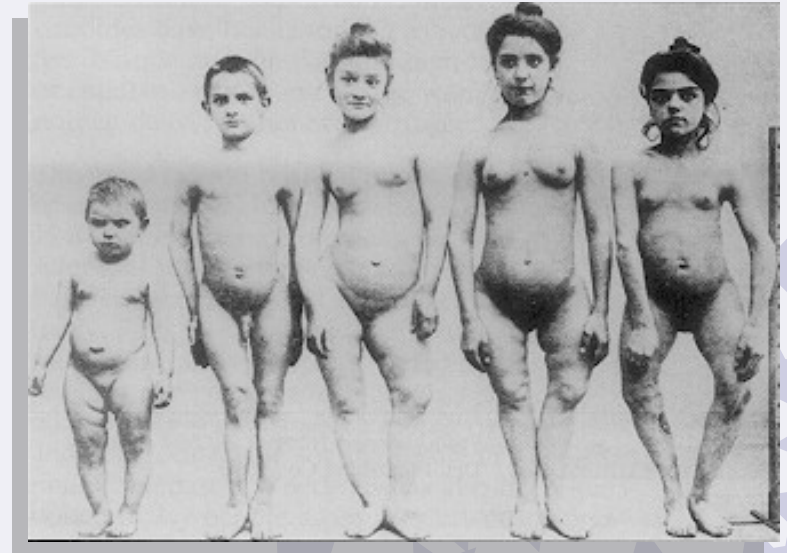
Summary: Sources to Achieve Normal Vitamin D Levels

♠ Sunlight: UV B —270-290 nm

- **10 minutes** of summer sun over the weekend without sunblock makes ~10,000 IU of Vitamin D (25 times %DV)
- Those in Northern Latitudes have lower Vitamin D levels
- African Americans and Hispanics in Northern latitudes have lower Vitamin D levels because of darker complexion

♠ Diet: %DV: **400 IU** = 0.01 mgms Dose)

- Fortified Dairy Products
 - **1 Cup Milk = ~100 IU**
- Fish (Cod Liver Oil, Salmon)
- Fortified Cereal
 - $\frac{3}{4}$ Cup serving = 40 IU



Rickets photo courtesy of the NIH

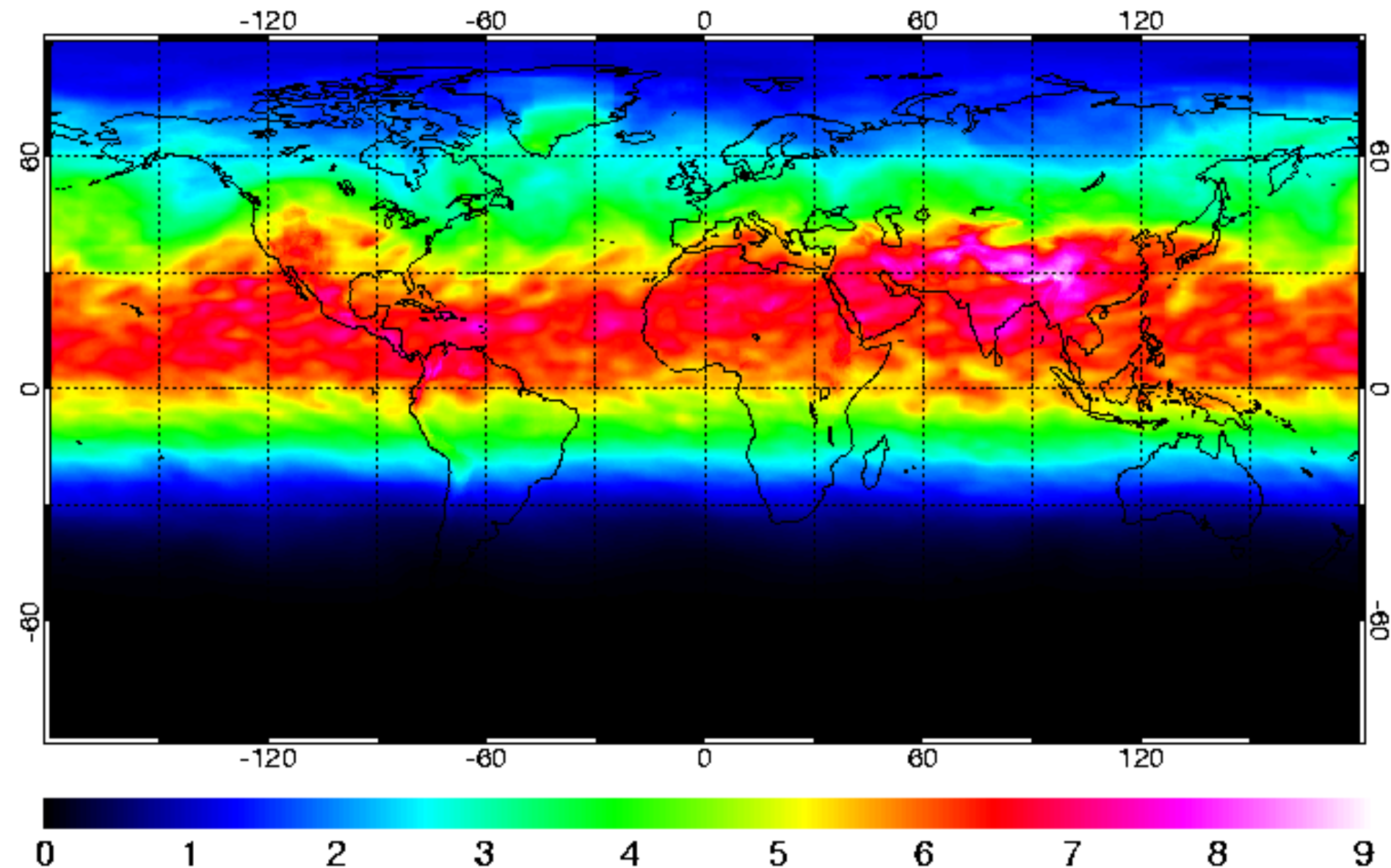
Vitamin-D UV dose (kJ/m²)

SCIAMACHY - KNMI/ESA

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Clear-sky

21 June 2007



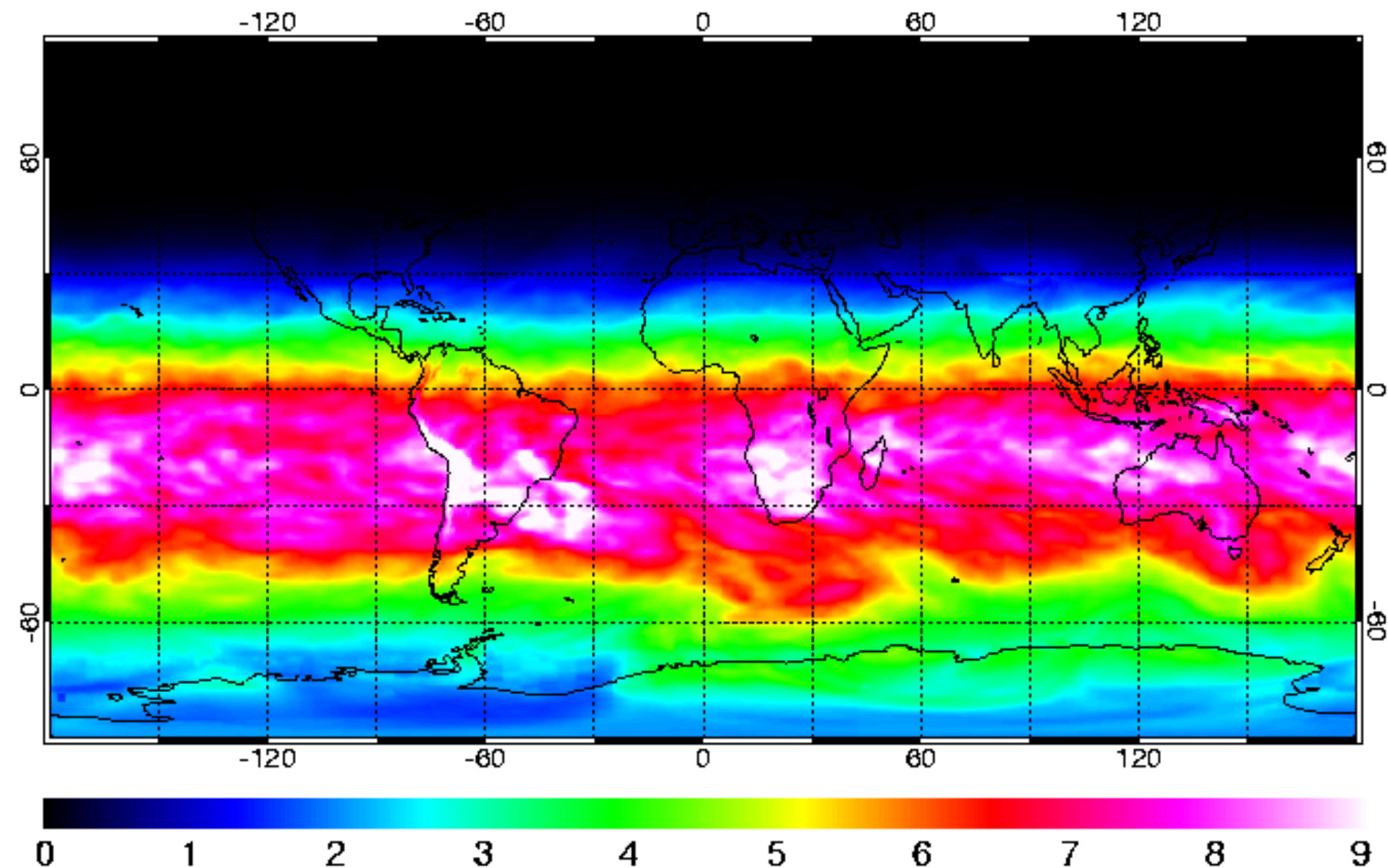
Vitamin-D UV dose (kJ/m²)

SCIAMACHY - KNMI/ESA

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Clear-sky

21 December 2006



Definition of Vitamin D Deficiency and Insufficiency Based on Blood Measurements of 25 OH Vitamin D



Adapted from Hollis, Journal of Nutrition 2005, 135:317-322

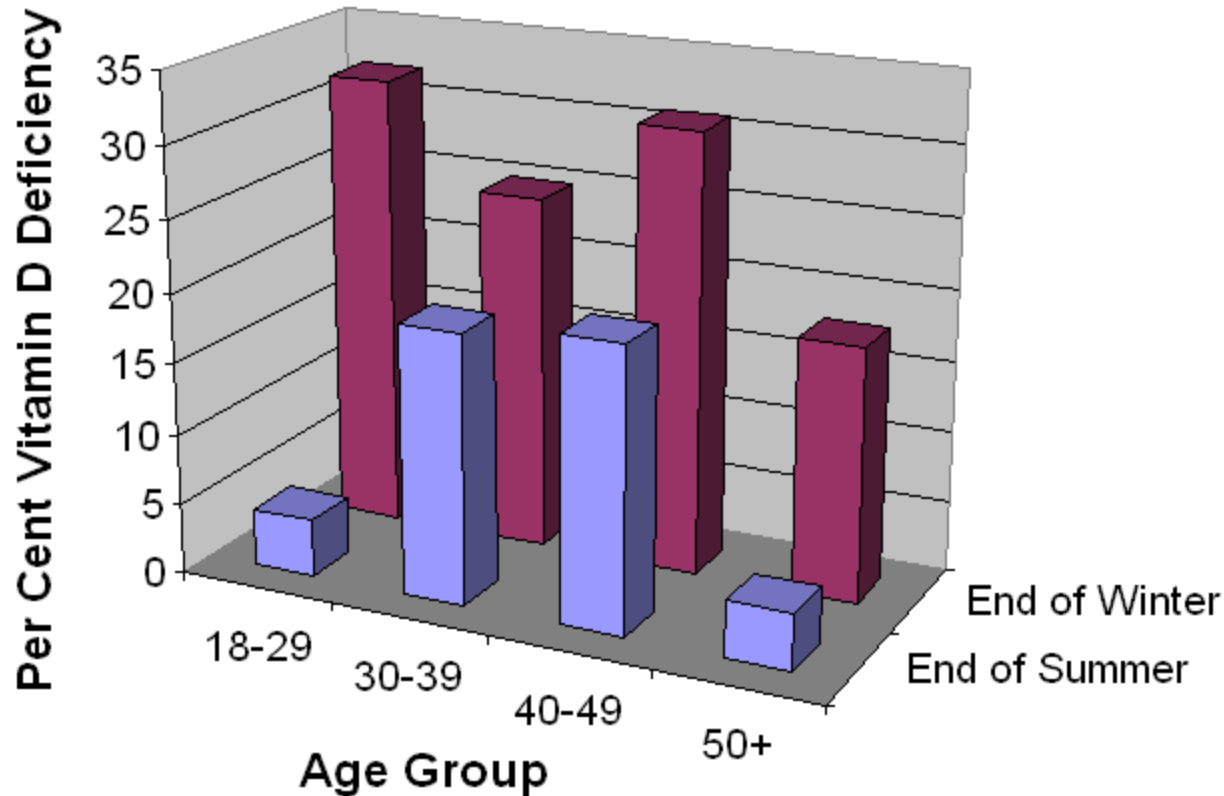
- ♠ Vitamin D **Sufficiency**: ≥ 32 ng/ml
 - Vitamin D **Low Normal or Insufficiency**
(when PTH levels begin to rise): **20 — <32** ng/ml
- ♠ Vitamin D **Deficiency**: **<20** ng/ml
- ♠ Measurements performed by **HPLC, RIA, or Chemiluminescence**

Is there Vitamin D Deficiency in the Military?



- ♠ **Prevalent in the general adult population**
- ♠ **Present in the Finnish military and associated with stress fractures**
- ♠ **2 month prophylaxis of U.S. female Navy recruits with Vitamin D (plus Calcium) reduces stress fractures**
- ♠ **Service members with chronic pain referred to the DHCC have Vitamin D deficiency**

Prevalence of Vitamin D Deficiency in Healthy Adults (Boston)



Tangpricha, Pearce, Chen, and Holick. The American Journal of Medicine. 2002. Vol 112. pp 659-662

Association Between Serum 25 (OH)D Concentrations and Bone Stress Fractures in Finnish Young Men



Ruhola et al. Journal of Bone and Mineral Research 2006 21(9):1483

- ♠ Prospective study of 800 Finnish male military recruits
 - **756 recruits completed 90 days of observation**
 - Stress fractures confirmed by X-ray
- ♠ **3.7%** were **< 16 ng/ml** (Finnish deficiency norm)
- ♠ **2.9% (22) developed stress fractures**
 - **11.6 stress fractures per 100 person years**
 - Distribution: **43% tibia** (13); **33% metatarsals** (10); 10% calcaneus (3); 7% navicular (2)
- ♠ Those < 31 ng/ml (median) had significantly higher stress fracture risk than those >31 ng/ml
 - **Overall increased risk was 3.6** (95% CI: 1.2-11.1)

Vitamin D/Calcium Supplements



Reduce Stress Fractures in Navy Recruits

Lappe, Cullen, Recker, Thompson, and Ahlf

33rd Annual Orthopaedic Research Society Meeting

San Diego, February 11, 2007

♠ **5,201 female Navy recruits** studied for 60 days while in basic training. **3,700 completed** study.

- Ages 17-35; Vitamin D not measured
- Received **800 IU of Vitamin D** and 2,000 mg of calcium daily, or placebo
- 170 stress fractures (~**30 stress fractures per 100 person years**) in the placebo group versus
- ~127 stress fractures in supplemental group (~**22 stress fractures per 100 person years**)

Prevalence of Severe Hypovitaminosis D in Patients With Persistent, Nonspecific Musculoskeletal Pain



Plotnikoff and Quigley, Mayo Clin Proc. 2003;78:1463-1470

- ♠ **150 consecutive patients** (ages 10-65 years) with **non-specific musculoskeletal pain**
- ♠ **93% had vitamin D levels below 20 ng/ml**
- ♠ Vitamin D deficient individuals were disproportionately **women, African Americans, Native Americans, and Hispanics**
- ♠ Pathophysiology: unclear
- ♠ **Conclusion: screen persistent nonspecific musculoskeletal pain for Vitamin D deficiency as standard care**

Fracture and Vitamin D Deficiency

Case Study 1



- ♠ 26 year old male of **Middle Eastern** heritage with 2 1/2 years of service, **lived in Northern U.S.** last 9 years. **Lactose intolerance.**
- ♠ Sustained **stress fracture of left tibia** during training (AIT).
 - X-rays reveal stress fracture at 4 weeks. Placed in cast for 12 weeks. Cast removed and given tramadol for **chronic pain.**
- ♠ Deployment to Iraq
 - Exposed to 5 blasts, **2 with brief loss of consciousness**
 - Changed to Percocet for pain, later evacuated for **acute psychosis**
- ♠ Psychosis resolved and **bone scan revealed non-union of stress fracture at 17 months.**
- ♠ Patient referred to Deployment Health Clinical Center
 - **PTSD, anxiety, and co-morbid chronic left tibial pain.**
- ♠ Screening 17 months after fracture: **vitamin D level of 11 ng/ml** (normal > 20)

Fracture and Vitamin D Deficiency

Case Study 2



- ♠ **36 year old African American** with 6 years of service, signed up after 9/11 while living in the **northern U.S.**
- ♠ **Deployment to Iraq**
 - **3rd month:** rolled off cot during mortar attack and **injured right wrist**. Negative X-rays. Conservative measures for **chronic pain**.
 - **4th month: re-injured right wrist** when 84 pound gun was dropped on it.
 - **9th month: chronic pain leads to medical evacuation**
- ♠ **Arthroscopy** performed with some improvement in pain, Conservative management continued.
- ♠ **Nuclear scan for chronic pain** 7 months after injury:
 - **stress changes in lunate wrist bone and posttraumatic changes in triquetrum**. Conservative management remains indicated.
- ♠ Patient referred to Deployment Health Clinical Center for co-morbid PTSD, anxiety, and chronic right wrist pain.
- ♠ Screening 14 months after injury: **vitamin D level of 12**



Vitamin D Deficiency at the Deployment Health Clinical Center



- ♠ Of **94** referrals seen from March 2005 until September 2006, 83 (88%) were screened.
 - **> 90% with chronic musculoskeletal pain**
 - Either multiple unexplained physical symptoms or PTSD, or PTSD-mild TBI overlap. 14 with fibromyalgia.
 - Most OIF/OEF veterans, and many with deployment related musculoskeletal injuries.
- ♠ **46%** (n= 38) have low Vitamin D (<20 ng/ml)
 - Average for those deficient: **13** ng/ml (range: 6-19)

Possible Reasons for Vitamin Deficiency in Recently Deployed OIF/OEF Veterans



♠ During Deployment

- **Lack of sun** because of protective measures
 - Sleeves worn down
 - Sunscreen use on exposed skin
 - Shade/Cover seeking behavior
 - Night time operational requirements
- **Lack of fortified dairy products consumption**
 - May not be available downrange, or not the first choice as a refreshment
 - Fortified dairy products not in MREs: Average MRE has ~80 IU of Vitamin D

Possible Reasons for Vitamin Deficiency in Recently Deployed OIF/OEF Veterans (continued)



♠ After Deployment

- Anxiety, PTSD, leads to avoidance behavior precluding outdoor activities in the sun
- PTSD associated with photophobia leading to avoidance of sunlight
- Convalescence after injury leads to indoor activities

More Vitamin D

Pathophysiology: Beyond the “Bare Bones”



- ♠ Pathophysiology for the association of chronic pain and Vitamin D Deficiency is not known
- ♠ However, Vitamin D receptors have been recognized in the CNS, as well in many other tissues, suggesting vitamin D has essential functions as a hormone outside of bone metabolism
- ♠ Chronic pain has been associated with CNS dysfunction
- ♠ Vitamin D receptor knock-out mice demonstrate anxiety behaviors

More Vitamin D Pathophysiology: Beyond the “Bare Bones” (continued)



- ♠ **Vitamin D Deficiency has been implicated in:**
 - **Cancer susceptibility**
 - Prostate Cancer (more common in Northern latitudes)
 - Colon Cancer (more common in Northern latitudes)
 - **Immune dysfunction/Autoimmune disease**
 - Tuberculosis treatment with sunlight
 - Multiple Sclerosis (more common in Northern latitudes)
 - **Diabetes susceptibility**
 - **Anxiety and Depression in Fibromyalgia**
 - Vitamin D deficiency is associated with anxiety and depression in fibromyalgia
Armstrong et al. Clin Rheumatol. 2007 Apr;26(4):551-4.
 - Question: Any correlation of vitamin D deficiency with anxiety and/or depression in patients with chronic pain and/or PTSD?

Treating Vitamin D Insufficiency/Deficiency



♠ 50,000 IU of Vitamin D once a week for 8 weeks

Holick, Mayo Clin Proc. 2003;78:1457-1459

♠ Side Effects:

- Nausea, vomiting, poor appetite, weight loss, constipation, weakness
- Confusion or arrhythmias with concomitant increase in serum calcium
- Soft tissue calcinosis (with toxic amounts of Vitamin D) e.g., in the kidney
 - Caution in sarcoidosis, oat cell lung cancer, non-Hodgkin's lymphoma

Conclusions: Force Health Protection Implications



- ♠ Service members with **stress fractures and/or chronic pain syndromes should be screened** for low vitamin D levels
- ♠ More studies needed: to determine Vitamin D deficiency prevalence in the military and possible links to other co-morbidities.
 - Non-healing fractures, chronic pain, anxiety, depression, PTSD, and PTSD-mild TBI overlap
 - **Can supplementation help co-morbidities?**